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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/809,877	03/26/2004	Malford E. Cullum	NC 84,641	7806

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EXAMINER	
GRASER, JENNIFER E	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/809,877	CULLUM ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *3, 4 and 16-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 5-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 March 2004* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1, 2 and 5-15 and 28, species A, detection of protective antigen by fluorescence polarization, in the reply filed on 7/18/07 is acknowledged. The traversal is on the ground(s) that both Groups are in Class 435 and that there is a limited prior art search that would not place a serious burden on the Examiner. This is not found persuasive because Class 435 contains over 300+ subclasses covering a very wide range of inventions, e.g, vectors, apparatus, plant cells, etc. so the fact that two inventions are in the same Class, not Class **and** subclass by no means indicates that they are closely related. Additionally, Inventions Group I and Group II are directed to related to determining the presence of a protein with a competitive assay and determining the presence of an antibody with a fluorochrome labeled binding reagent, respectively. The related inventions are distinct if the (1)the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP §806.05fj). In the instant case, the inventions as claimed the method of Group II has a materially different design by only adding a single reagent to sample while the method of Group I adds two reagents to the sample which results in determining the presence or absence of different products in the sample, specifically the mode of operation in Group I is clearly competitive and the mode of operation is between a labeled reagent and the antibody in the sample, no competition

between components is required as now claimed, therefore, the methods of each group function differently and effectively determine the presence of structurally different products in the sample, one product being a protein of Bacillus anthracis and the other being an antibody that binds to an antigen of the pathogen; (2) the inventions do not overlap in scope because each method determines the presence or absence of products that structurally, and functionally are distinct based upon differing amino acid structures and the binding specificities conferred to the products based upon these structures. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different sub-classification and their recognized divergent subject matter and because the literature search required for the Groups is not coextensive and it would place a serious burden on the Examiner to examine the Groups together, restriction for examination purposes as indicated is proper.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 2, 3 (non-elected species) and 16-27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claim Rejections - 35 USC § 112-2nd paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1, 2, 5-15 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "said B.anthracis polypeptide" in line 3. There is insufficient antecedent basis for this limitation in the claim. The preamble does not recite a B.anthracis polypeptide, e.g., it recites 'estimating the concentration in a sample of B.anthracis", not 'estimating the concentration in a sample of B.anthracis polypeptide'.

Claim 1, step (a) is vague and confusing because it is unclear what is being mixed together, e.g, is it sample, antibody to B.anthracis polypeptide which is suspected to be in the sample, and ***any*** B.anthracis polypeptide labeled with a fluorchrome? Or, is the polypeptide labeled with the fluorochrome also the same B.anthracis polypeptide which is suspected of being in the sample? Clarification and correction is requested.

Claim 1, step (c) is vague and confusing because it is unclear which binding interaction is being detected. The claim recites that it is detecting binding between the B.anthracis polypeptide and antibody. Which B.anthracis polypeptide is being referred to? Is the antibody binding the B.anthracis poypeptide labeled with fluorochrome being detected or the antibody binding the B.anthracis polypeptide suspected of being in the sample, or a complex of all three? Clarification and correction is requested.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: there is no correlation step between the

detection of binding interaction in part (c) and the estimating the concentration in a sample of a B.anthracis bacterium in the preamble. The claim fails to provide correlation from step (c) back to the preamble. There is no estimation of concentration at the end of the method.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: there is no control step in the method. Fluorescence polarization requires a baseline in order to work properly.

Claim 2 is vague and indefinite because it is unclear what change is be detected and what the specific change indicates about the concentration of B.anthracis in a sample.

Claim 5 is vague and confusing because it recites either just a negative control or a positive control may be used or they both may be used. It is unclear how the assay would function properly without both a positive and a negative control solution.

Claim 7 is vague and indefinite because there is no correlation step between the detection of binding interaction in part (c) and the estimating the concentration in a sample of a B.anthracis bacterium in the preamble. It is unclear how this protein detection correlates to the estimation of B.anthracis bacterium. Additionally, it appears a binding interaction is being detected, not a specific concentration of protein in claim 1.

Claims 9 and 10 are vague and indefinite because it is unclear what is meant by a 'concentrated' or 'unconcentrated' sample. What is the sample concentrated or unconcentrated with?

Claim 13 is vague and confusing because there is no reference to 'sample millipolarization' in claim 1 from which it depends.

Claim 15 is vague and indefninte because it is unclear what is encompassed by "other clinical and laboratory specimens and samples'. It is unclear what other bodily fluids besides the ones recited in claim 15 would be encompassed by this definition. The metes and bounds of "other clinical and laboratory specimens and samples' cannot be understood. Clarification and correction is requested.

Claim Objections

4. Claims 1, 6 and 28 are objected to because of the following informalities: they contain non-elected subject matter which must be removed from the claim, e.g., claim 1 has non-elected species fluorescence lifetime or fluorescence resonance energy transfer in the last line, claim 6 contains non-elected protein fragments and claim 28 contains non-elected protein species. Appropriate correction is required.

Claim Rejections - 35 USC § 112-Scope of Enablement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims1, 2 and 5-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for fluorescence polarization assays which use protective antigen from B.anthracis for the detection of B.anthracis, does not reasonably provide enablement for methods which use *any* polypeptide from B.anthracis for estimating the concentration in a sample of B.anthracis. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The instant claims broadly read on the use of *any* B.anthracis polypeptide "for estimating the concentration in a sample of B.anthracis". The prior art teaches that in order for a bacterial diagnostic assay to be successful the detection reagent must be one which is conserved across the Genus/species of the bacterium. Additionally, fluorescence polarization assays place limitations on the antigen which is to be used, e.g., the size of the antigen, its ability to be covalently linked with a fluorochrome and its ability to induce an antibody response in exposed animals. See page 167 of Nielsen et al (J.Immunolg. Methods. 1996. 195: 161-168). Accordingly, it would take one of skill in the art undue experimentation to discover an antigen which would be successful in the claimed methods. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." The claims should be limited to the elected species, e.g., protective antigen.

Additionally, the method as claimed recites "a competitive method for estimating the concentration in a sample of a Bacillus anthracis", yet the method recited in the claims appears to solely be detecting B.anthracis polypeptide. There is no description or correlation of B.anthracis quantitation in either the claimed method or the instant specification. Accordingly, the methods as claimed are not enabled.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 2, 5-15 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tencza et al (J.Clin.Microbiol. May 2000. 38(5): 1854-1859) and Nielsen et al (J.Immunolg. Methods. 1996. 195: 161-168) in view of Simonson et al (US 6,927,068 B2).

Tencza et al teach the development of a fluorescence polarization-based diagnostic assay for equine infectious anemia virus. The reference teaches that FP (fluorescence polarization) has been used as a tool to monitor protein-protein, protein-peptide, and other intermolecular reactions. Tencza et al teach that advances in intstrumentation allowed for rapid immunassays for a large number of analytes including therapeutic druges and metabolites, as well as antibodies to infectious agents. These FP assays can be performed in a matter of minutes (versus hours or days for other tests, such as ELISAs) and usually do not require extensive sample preparation. See

page 1855, column 1. Additionally, it is taught that the materials required for the assay are relatively simple and highly simple, making FP attractive for field use. Negative and positive controls were used in the assay, see paragraph bridging pages 1855-1856.

Nielsen et al teach a homogenous fluorescence polarization assay for detection of antibody to Brucella abortus. A negative control was used in the assay. See abstract. Nielsen teach that fluorescence polarization has been known as early as 1981, see page 162, top of column 2. Nielsen eta l teache a single, one-step serum dilution on which a baseline serum intensity blank is obtained using a fluorescene polarization analyzer. This is followed by the addition of fluorescein labeled B.abortus O-polysaccharide tracer. The fluorescence polarization of the tracer is then measured. The total time for the assay is approximately 2 minutes. Nielsen et al teach that the FP assay was highly accurate and due to the ease and rapidity of the procedure, it is quite likely that it could be adapted as a field test at a considerable cost reduction over other primary binding assays. It is stated that procedure is quite possible adaptable to testing exposure to other pathogens, the only limitations being the size of the antigen, its ability to be covalently linked with a fluorochrome and its ability to induce an antibody response in exposed animals. See page 167.

However, Tencza and Nielsen do not particularly teach using a B.anthracis polypeptide, particularly protective antigen, in their assay methods.

Simonson et al teach a rapid and non-invasive method to detect the presence of protective antigen (PA) from B.anthracis. The reference teaches that PA was a very well-known prominent antigen from B.anthracis which has long been a target of

diagnostic assays. Simonson teach a competitive immunoassay which includes mixing a body fluid sample suspected of exposure to B.anthracis with a labeled B.anthracis polypeptide. Body fluid samples are taught to include: saliva, oral rinse expectorant, oral fluid including oral mucosal transudate and gingival crevicular fluid, urine, sweat, tears, blood, serium, stool, etc., see column 9, lines 14-22.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made that protective antigen from B.anthracis could be used in a fluorescence polarization assay as outlined by Tencza or Nielsen above because the prior art teaches that PA has long been a diagnostic target of B.anthracis and there was a need in the prior art for rapid indentification of the polypeptide and/or antibodies which bind to PA. . Nielsen et al specifically teach that the FP assay was highly accurate and due to the ease and rapidity of the procedure, it is quite likely that it could be adapted as a field test at a considerable cost reduction over other primary binding assays. It is stated that procedure is quite possible adaptable to testing exposure to other pathogens, the only limitations being the size of the antigen, its ability to be covalently linked with a fluorochrome and its ability to induce an antibody response in exposed animals. Since PA clearly was known to meet all of the criteria it would have been obvious for one of ordinary skill in the art to use it in an FP assay and one would have been highly motivated to do so since it could be adapted as a field test at a considerable cost reduction over other primary binding assays and it is an extremely rapid procedure which would save time in the field. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a

result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 9, 10 and 13 are for any particular purpose or solve any stated problem and the prior art teaches that FP methods often vary according to the sample being analyzed and various matrices, solutions and parameters appear to work equally as well, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the prior art by normal optimization procedures known in the FP art.

Prior art made of record, not relied on:

Cunningham et al (US 6,955,891 B2),

Cunningham et al teach methods for assaying a B.anthracis polypeptide, i.e., lethal factor protease. The reference teaches detection by fluorescence resonance energy transfer.

9. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 7:30 AM-6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached on (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

Jennifer Graser
Primary Examiner
Art Unit 1645

9/12/07